



COPY OF PAPERS
ORIGINALLY FILED

SEQUENCE LISTING

<110> Bristol-Myers Squibb Company
<120> AGGRECAN DEGRADING METALLO PROTEASES
<130> DM6909B
<160> 21
<170> PatentIn version 3.0
<210> 1
<211> 4192
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> (406)..(2916)

<400> 1
acagacacat atgcacgaga gagacagagg aggaagaga cagagacaaa ggcacagcg 60
aagaaggcag agacagggca ggcacagaag cggcccgac agagtctac agagggagag 120
gccagagaag ctgcagaaga cacaggcagg gagagacaaa gatccaggaa aggagggctc 180
aggaggagag tttggagaag ccagaccctt gggcacctct cccaagccc aggactaagt 240
tttctccatt tccttaacg gtcctcagcc cttctaaaaa ctttgcctct gaccttgca 300
ggagtccaaag cccccaggct acagagagga gctttccaaa gctagggtgt ggaggacttg 360
gtgccctaga cggcctcagt ccctcccagc tgcaatcca gtgcc atg tcc cag aca 417
Met Ser Gln Thr
1

ggc tcg cat ccc ggg agg ggc ttg gca ggg cgc tgg ctg tgg gga gcc 465
Gly Ser His Pro Gly Arg Gly Leu Ala Gly Arg Trp Leu Trp Gly Ala
5 10 15 20

caa ccc tgc ctc ctg ctc ccc att gtg ccg ctc tcc tgg ctg gtg tgg 513
Gln Pro Cys Leu Leu Pro Ile Val Pro Leu Ser Trp Leu Val Trp
25 30 35

ctg ctt ctg cta ctg ctg gcc tct ctc ctg ccc tca gcc cgg ctg gcc 561
Leu Leu Leu Leu Leu Ala Ser Leu Leu Pro Ser Ala Arg Leu Ala
40 45 50

agc ccc ctc ccc cgg gag gag gag atc gtg ttt cca gag aag ctc aac 609

RECEIVED

FEB 22 2002

TECH CENTER 1600/2900

INS
C

B

NS
A

Ser Pro Leu Pro Arg Glu Glu Glu Ile Val Phe Pro Glu Lys Leu Asn	55	60	65	
ggc agc gtc ctg cct ggc tcg ggc gcc cct gcc agg ctg ttg tgc cgc				657
Gly Ser Val Leu Pro Gly Ser Gly Ala Pro Ala Arg Leu Leu Cys Arg				
70	75	80		
ttg cag gcc ttt ggg gag acg ctg cta cta gag ctg gag cag gac tcc				705
Leu Gln Ala Phe Gly Glu Thr Leu Leu Leu Glu Leu Glu Gln Asp Ser				
85	90	95	100	
ggt gtg cag gtc gag ggg ctc aca gtg cag tac ctg ggc cag gcg cct				753
Gly Val Gln Val Glu Gly Leu Thr Val Gln Tyr Leu Gly Gln Ala Pro				
105	110	115		
gag ctg ctg ggt gga gca gag cct ggc acc tac ctg act ggc acc atc				801
Glu Leu Leu Gly Gly Ala Glu Pro Gly Thr Tyr Leu Thr Gly Thr Ile				
120	125	130		
aat gga gat ccg gag tcg gtg gca tct ctg cac tgg gat ggg gga gcc				849
Asn Gly Asp Pro Glu Ser Val Ala Ser Leu His Trp Asp Gly Gly Ala				
135	140	145		
ctg tta ggc gtg tta caa tat cgg ggg gct gaa ctc cac ctc cag ccc				897
Leu Leu Gly Val Leu Gln Tyr Arg Gly Ala Glu Leu His Leu Gln Pro				
150	155	160		
ctg gag gga ggc acc cct aac tct gct ggg gga cct ggg gct cac atc				945
Leu Glu Gly Gly Thr Pro Asn Ser Ala Gly Gly Pro Gly Ala His Ile				
165	170	175	180	
cta cgc cgg aag agt cct gcc agc ggt caa ggt ccc atg tgc aac gtc				993
Leu Arg Arg Lys Ser Pro Ala Ser Gly Gln Gly Pro Met Cys Asn Val				
185	190	195		
aag gct cct ctt gga agc ccc agc ccc aga ccc cga aga gcc aag cgc				1041
Lys Ala Pro Leu Gly Ser Pro Ser Pro Arg Pro Arg Arg Ala Lys Arg				
200	205	210		
ttt gct tca ctg agt aga ttt gtg gag aca ctg gtg gtg gca gat gac				1089
Phe Ala Ser Leu Ser Arg Phe Val Glu Thr Leu Val Val Ala Asp Asp				
215	220	225		
aag atg gcc gca ttc cac ggt gcg ggg cta aag cgc tac ctg cta aca				1137
Lys Met Ala Ala Phe His Gly Ala Gly Leu Lys Arg Tyr Leu Leu Thr				
230	235	240		
gtg atg gca gca gca gcc aag gcc ttc aag cac cca agc atc cgc aat				1185
Val Met Ala Ala Ala Lys Ala Phe Lys His Pro Ser Ile Arg Asn				
245	250	255	260	
cct gtc agc ttg gtg gtg act cgg cta gtg atc ctg ggg tca ggc gag				1233
Pro Val Ser Leu Val Val Thr Arg Leu Val Ile Leu Gly Ser Gly Glu				
265	270	275		
gag ggg ccc caa gtg ggg ccc agt gct gcc cag acc ctg cgc agc ttc				1281
Glu Gly Pro Gln Val Gly Pro Ser Ala Ala Gln Thr Leu Arg Ser Phe				

280 285 290

tgt gcc tgg cag cg~~g~~ ggc ctc aac acc cct gag gac tcg gac cct gac 1329
Cys Ala Trp Gln Arg Gly Leu Asn Thr Pro Glu Asp Ser Asp Pro Asp
295 300 305

cac ttt gac aca g~~c~~ att ctg ttt acc cgt cag gac ctg tgt gga gtc 1377
His Phe Asp Thr Ala Ile Leu Phe Thr Arg Gln Asp Leu Cys Gly Val
310 315 320

tcc act tgc gac acg ctg ggt atg gct gat gtg ggc acc gtc tgt gac 1425
Ser Thr Cys Asp Thr Leu Gly Met Ala Asp Val Gly Thr Val Cys Asp
325 330 335 340

ccg gct cgg agc tgt g~~c~~ att gtg gag gat gat ggg ctc cag tca gcc 1473
Pro Ala Arg Ser Cys Ala Ile Val Glu Asp Asp Gly Leu Gln Ser Ala
345 350 355

ttc act gct cat gaa ctg ggt cat gtc ttc aac atg ctc cat gac 1521
Phe Thr Ala Ala His Glu Leu Gly His Val Phe Asn Met Leu His Asp
360 365 370

aac tcc aag cca tgc atc agt ttg aat ggg cct ttg agc acc tct cgc 1569
Asn Ser Lys Pro Cys Ile Ser Leu Asn Gly Pro Leu Ser Thr Ser Arg
375 380 385

cat gtc atg gcc cct gtg atg gct cat gtg gat cct gag gag ccc tgg 1617
His Val Met Ala Pro Val Met Ala His Val Asp Pro Glu Glu Pro Trp
390 395 400

tcc ccc tgc agt gcc cgc ttc atc act gac ttc ctg gac aat ggc tat 1665
Ser Pro Cys Ser Ala Arg Phe Ile Thr Asp Phe Leu Asp Asn Gly Tyr
405 410 415 420

ggg cac tgt ctc tta gac aaa cca gag gct cca ttg cat ctg cct gtg 1713
Gly His Cys Leu Leu Asp Lys Pro Glu Ala Pro Leu His Leu Pro Val
425 430 435

act ttc cct ggc aag gac tat gat gct gac cgc cag tgc cag ctg acc 1761
Thr Phe Pro Gly Lys Asp Tyr Asp Ala Asp Arg Gln Cys Gln Leu Thr
440 445 450

ttc ggg ccc gac tca cgc cat tgt cca cag ctg ccg ccg ccc tgt gct 1809
Phe Gly Pro Asp Ser Arg His Cys Pro Gln Leu Pro Pro Pro Cys Ala
455 460 465

gcc ctc tgg tgc tct ggc cac ctc aat ggc cat gcc atg tgc cag acc 1857
Ala Leu Trp Cys Ser Gly His Leu Asn Gly His Ala Met Cys Gln Thr
470 475 480

aaa cac tcg ccc tgg gcc gat ggc aca ccc tgc ggg ccc gca cag gdc 1905
Lys His Ser Pro Trp Ala Asp Gly Thr Pro Cys Gly Pro Ala Gln Ala
485 490 495 500

tgc atg ggt ggt cgc tgc ctc cac atg gac cag ctc cag gac ttc aat 1953
Cys Met Gly Gly Arg Cys Leu His Met Asp Gln Leu Gln Asp Phe Asn
505 510 515

INS
CL

att cca cag gct ggt ggc tgg ggt cct tgg gga cca tgg ggt gac tgc 2001
Ile Pro Gln Ala Gly Gly Trp Gly Pro Trp Gly Pro Trp Gly Asp Cys
520 525 530

tct cgg acc tgt ggg ggt gtc cag ttc tcc tcc cga gac tgc acg 2049
Ser Arg Thr Cys Gly Gly Val Gln Phe Ser Ser Arg Asp Cys Thr
535 540 545

agg cct gtc ccc cgg aat ggt ggc aag tac tgt gag ggc cgc cgt acc 2097
Arg Pro Val Pro Arg Asn Gly Gly Lys Tyr Cys Glu Gly Arg Arg Thr
550 555 560

cgc ttc cgc tcc tgc aac act gag gac tgc cca act ggc tca gcc ctg 2145
Arg Phe Arg Ser Cys Asn Thr Glu Asp Cys Pro Thr Gly Ser Ala Leu
565 570 575 580

acc ttc cgc gag gag cag tgt gct gcc tac aac cac cgc acc gac ctc 2193
Thr Phe Arg Glu Glu Gln Cys Ala Ala Tyr Asn His Arg Thr Asp Leu
585 590 595

ttc aag agc ttc cca ggg ccc atg gac tgg gtt cct cgc tac aca ggc 2241
Phe Lys Ser Phe Pro Gly Pro Met Asp Trp Val Pro Arg Tyr Thr Gly
600 605 610

gtg gcc ccc cag gac cag tgc aaa ctc acc tgc cag gcc cgg gca ctg 2289
Val Ala Pro Gln Asp Gln Cys Lys Leu Thr Cys Gln Ala Arg Ala Leu
615 620 625

ggc tac tac tat gtg ctg gag cca cgg gtg gta gat ggg acc ccc tgt 2337
Gly Tyr Tyr Tyr Val Leu Glu Pro Arg Val Val Asp Gly Thr Pro Cys
630 635 640

tcc ccg gac agc tcc tcg gtc tgt gtc cag ggc cga tgc atc cat gct 2385
Ser Pro Asp Ser Ser Val Cys Val Gln Gly Arg Cys Ile His Ala
645 650 655 660

ggc tgt gat cgc atc att ggc tcc aag aag aag ttt gac aag tgc atg 2433
Gly Cys Asp Arg Ile Ile Gly Ser Lys Lys Lys Phe Asp Lys Cys Met
665 670 675

gtg tgc gga ggg gac ggt tct ggt tgc agc aag cag tca ggc tcc ttc 2481
Val Cys Gly Gly Asp Gly Ser Gly Cys Ser Lys Gln Ser Gly Ser Phe
680 685 690

agg aaa ttc agg tac gga tac aac aat gtg gtc act atc ccc gcg ggg 2529
Arg Lys Phe Arg Tyr Gly Tyr Asn Asn Val Val Thr Ile Pro Ala Gly
695 700 705

gcc acc cac att ctt gtc cgg cag cag gga aac cct ggc cac cgg agc 2577
Ala Thr His Ile Leu Val Arg Gln Gln Gly Asn Pro Gly His Arg Ser
710 715 720

atc tac ttg gcc ctg aag ctg cca gat ggc tcc tat gcc ctc aat ggt 2625
Ile Tyr Leu Ala Leu Lys Leu Pro Asp Gly Ser Tyr Ala Leu Asn Gly
725 730 735 740

gaa tac acg ctg atg ccc tcc ccc aca gat gtg gta ctg cct ggg gca 2673
 Glu Tyr Thr Leu Met Pro Ser Pro Thr Asp Val Val Leu Pro Gly Ala
 745 750 755

gtc agc ttg cgc tac agc ggg gcc act gca gcc tca gag aca ctg tca 2721
 Val Ser Leu Arg Tyr Ser Gly Ala Thr Ala Ala Ser Glu Thr Leu Ser
 760 765 770

ggc cat ggg cca ctg gcc cag cct ttg aca ctg caa gtc cta gtg gct 2769
 Gly His Gly Pro Leu Ala Gln Pro Leu Thr Leu Gln Val Leu Val Ala
 775 780 785

ggc aac ccc cag gac aca cgc ctc cga tac agc ttc ttc gtg ccc cgg 2817
 Gly Asn Pro Gln Asp Thr Arg Leu Arg Tyr Ser Phe Phe Val Pro Arg
 790 795 800

ccg acc cct tca acg cca cgc ccc act ccc cag gac tgg ctg cac cga 2865
 Pro Thr Pro Ser Thr Pro Arg Pro Thr Pro Gln Asp Trp Leu His Arg
 805 810 815 820

aga gca cag att ctg gag atc ctt cgg cgg cgc ccc tgg gcg ggc agg 2913
 Arg Ala Gln Ile Leu Glu Ile Leu Arg Arg Arg Pro Trp Ala Gly Arg
 825 830 835

aaa taacctcaact atccccggctg ccctttatgg gcaccggggc ctcggactta 2966
 Lys

gctgggagaa agagagagct tctgttgctg cctcatgcta agactcagtg gggaggggct 3026

gtgggcgtga gacctgcccc tcctctctgc cctaattgcgc aggctggccc tgccctggtt 3086

tcctgccctg ggaggcagtg atgggttagt ggatgaaagg ggctgacaga cagccctcca 3146

tctaaactgc cccctctgcc ctgcgggtca caggagggag gggaaaggca gggagggcct 3206

gggcccccagt tgtattttt tagtattttat tcacttttat tttagcaccag ggaaggggac 3266

aaggactagg gtcctggga acctgacccc tgaccctca tagccctcac cctggggcta 3326

ggaaaatccag ggtggtggtg ataggtataa gtggtgtgtg tatgcgtgtg tgtgtgtgt 3386

tgaaaatgtg tgtgtgctta tgtatgaggt acaacctgtt ctgcatttctt cttcctgaat 3446

tttatttttt gggaaaagaa aagtcaaggg tagggtgggc cttcaggag tgagggatta 3506

tcctttttttt tttctttctt tctttctttt ttttttgag acagaatctc gctctgtcgc 3566

ccaggctgga gtgcaatggc acaatctcg ctcactgcat cctccggctc cgggttcaa 3626

gtgattctca tgcctcagcc tcctgagtag ctgggattac aggctcctgc caccacgccc 3686

ggctaattttt tttttgtttt tttttggaga cagagtctcg ctattgtcac caggctgga 3746

atgatttcag ctcactgcaa cttcgccac ctgggttcca gcaattctcc tgcctcagcc 3806

tccccgagtag ctgagattat aggcacctac caccacgccc ggctaattttt tttttttt 3866

gtagagacgg ggttcacca tggtggccag gctggtctcg aactcctgac ctttaggtat 3926
ccactcgccct tcatctccca aagtgcgtgg attacaggcg tgagccaccg tgcctggcca 3986
cgcccaacta attttgtat ttttagtaga gacagggttt caccatgttgc gccaggctgc 4046
tcttgaaactc ctgaccccttag gtaatcgacc tgcctcgcc tcccaaagtgc ctgggattac 4106
aggtgtgagc caccacgccc ggtacatatt ttttaaatttgc aattctacta tttatgttat 4166
cctttggag tcagacagat gtgggt 4192

<210> 2

<211> 837

<212> PRT

<213> Homo sapiens

<400> 2

Met Ser Gln Thr Gly Ser His Pro Gly Arg Gly Leu Ala Gly Arg Trp
1 5 10 15

Leu Trp Gly Ala Gln Pro Cys Leu Leu Leu Pro Ile Val Pro Leu Ser
20 25 30

Trp Leu Val Trp Leu Leu Leu Leu Ala Ser Leu Leu Pro Ser
35 40 45

Ala Arg Leu Ala Ser Pro Leu Pro Arg Glu Glu Glu Ile Val Phe Pro
50 55 60

Glu Lys Leu Asn Gly Ser Val Leu Pro Gly Ser Gly Ala Pro Ala Arg
65 70 75 80

Leu Leu Cys Arg Leu Gln Ala Phe Gly Glu Thr Leu Leu Leu Glu Leu
85 90 95

Glu Gln Asp Ser Gly Val Gln Val Glu Gly Leu Thr Val Gln Tyr Leu
100 105 110

Gly Gln Ala Pro Glu Leu Leu Gly Gly Ala Glu Pro Gly Thr Tyr Leu
115 120 125

Thr Gly Thr Ile Asn Gly Asp Pro Glu Ser Val Ala Ser Leu His Trp
130 135 140

Asp Gly Gly Ala Leu Leu Gly Val Leu Gln Tyr Arg Gly Ala Glu Leu
145 150 155 160

His Leu Gln Pro Leu Glu Gly Gly Thr Pro Asn Ser Ala Gly Gly Pro
165 170 175

Gly Ala His Ile Leu Arg Arg Lys Ser Pro Ala Ser Gly Gln Gly Pro

INS
C

180 185 190

Met Cys Asn Val Lys Ala Pro Leu Gly Ser Pro Ser Pro Arg Pro Arg
195 200 205

Arg Ala Lys Arg Phe Ala Ser Leu Ser Arg Phe Val Glu Thr Leu Val
210 215 220

Val Ala Asp Asp Lys Met Ala Ala Phe His Gly Ala Gly Leu Lys Arg
225 230 235 240

Tyr Leu Leu Thr Val Met Ala Ala Ala Lys Ala Phe Lys His Pro
245 250 255

Ser Ile Arg Asn Pro Val Ser Leu Val Val Thr Arg Leu Val Ile Leu
260 265 270

Gly Ser Gly Glu Glu Gly Pro Gln Val Gly Pro Ser Ala Ala Gln Thr
275 280 285

Leu Arg Ser Phe Cys Ala Trp Gln Arg Gly Leu Asn Thr Pro Glu Asp
290 295 300

Ser Asp Pro Asp His Phe Asp Thr Ala Ile Leu Phe Thr Arg Gln Asp
305 310 315 320

Leu Cys Gly Val Ser Thr Cys Asp Thr Leu Gly Met Ala Asp Val Gly
325 330 335

Thr Val Cys Asp Pro Ala Arg Ser Cys Ala Ile Val Glu Asp Asp Gly
340 345 350

Leu Gln Ser Ala Phe Thr Ala Ala His Glu Leu Gly His Val Phe Asn
355 360 365

Met Leu His Asp Asn Ser Lys Pro Cys Ile Ser Leu Asn Gly Pro Leu
370 375 380

Ser Thr Ser Arg His Val Met Ala Pro Val Met Ala His Val Asp Pro
385 390 395 400

Glu Glu Pro Trp Ser Pro Cys Ser Ala Arg Phe Ile Thr Asp Phe Leu
405 410 415

Asp Asn Gly Tyr Gly His Cys Leu Leu Asp Lys Pro Glu Ala Pro Leu
420 425 430

His Leu Pro Val Thr Phe Pro Gly Lys Asp Tyr Asp Ala Asp Arg Gln
435 440 445

Cys Gln Leu Thr Phe Gly Pro Asp Ser Arg His Cys Pro Gln Leu Pro
450 455 460

Pro Pro Cys Ala Ala Leu Trp Cys Ser Gly His Leu Asn Gly His Ala
465 470 475 480

Met Cys Gln Thr Lys His Ser Pro Trp Ala Asp Gly Thr Pro Cys Gly

INS
C1

485 490 495

Pro Ala Gln Ala Cys Met Gly Gly Arg Cys Leu His Met Asp Gln Leu
500 505 510

Gln Asp Phe Asn Ile Pro Gln Ala Gly Gly Trp Gly Pro Trp Gly Pro
515 520 525

Trp Gly Asp Cys Ser Arg Thr Cys Gly Gly Val Gln Phe Ser Ser
530 535 540

Arg Asp Cys Thr Arg Pro Val Pro Arg Asn Gly Gly Lys Tyr Cys Glu
545 550 555 560

Gly Arg Arg Thr Arg Phe Arg Ser Cys Asn Thr Glu Asp Cys Pro Thr
565 570 575

Gly Ser Ala Leu Thr Phe Arg Glu Glu Gln Cys Ala Ala Tyr Asn His
580 585 590

Arg Thr Asp Leu Phe Lys Ser Phe Pro Gly Pro Met Asp Trp Val Pro
595 600 605

Arg Tyr Thr Gly Val Ala Pro Gln Asp Gln Cys Lys Leu Thr Cys Gln
610 615 620

Ala Arg Ala Leu Gly Tyr Tyr Val Leu Glu Pro Arg Val Val Asp
625 630 635 640

Gly Thr Pro Cys Ser Pro Asp Ser Ser Ser Val Cys Val Gln Gly Arg
645 650 655

Cys Ile His Ala Gly Cys Asp Arg Ile Ile Gly Ser Lys Lys Phe
660 665 670

Asp Lys Cys Met Val Cys Gly Gly Asp Gly Ser Gly Cys Ser Lys Gln
675 680 685

Ser Gly Ser Phe Arg Lys Phe Arg Tyr Gly Tyr Asn Asn Val Val Thr
690 695 700

Ile Pro Ala Gly Ala Thr His Ile Leu Val Arg Gln Gln Gly Asn Pro
705 710 715 720

Gly His Arg Ser Ile Tyr Leu Ala Leu Lys Leu Pro Asp Gly Ser Tyr
725 730 735

Ala Leu Asn Gly Glu Tyr Thr Leu Met Pro Ser Pro Thr Asp Val Val
740 745 750

Leu Pro Gly Ala Val Ser Leu Arg Tyr Ser Gly Ala Thr Ala Ala Ser
755 760 765

Glu Thr Leu Ser Gly His Gly Pro Leu Ala Gln Pro Leu Thr Leu Gln
770 775 780

Val Leu Val Ala Gly Asn Pro Gln Asp Thr Arg Leu Arg Tyr Ser Phe

785 790 795 800

Phe Val Pro Arg Pro Thr Pro Ser Thr Pro Arg Pro Thr Pro Gln Asp
805 810 815

Trp Leu His Arg Arg Ala Gln Ile Leu Glu Ile Leu Arg Arg Arg Pro
820 825 830

Trp Ala Gly Arg Lys
835

<210> 4

<211> 26

<212> PRT

<213> Bos taurus

<400> 4

NCS

Phe Ala Ser Leu Ser Arg Val Glu Thr Leu Val Val Ala Asp Asp Lys
1 5 10 15

Met Ala Ala Phe His Gly Ala Gly Leu Lys
20 25

<210> 5

<211> 7

<212> PRT

<213> Bos taurus

<400> 5

Tyr Thr Gly Val Ala Pro Arg
1 5

<210> 6

<211> 11

<212> PRT

<213> Bos taurus

<400> 6

Ala Leu Gly Tyr Tyr Tyr Val Leu Asp Pro Arg
1 5 10

<210> 7

<211> 21

~~11~~ <212> DNA

<213> Mus musculus

<400> 7

gggggtggtg tccagttctc c

21

<210> 8

<211> 23

<212> DNA

<213> Mus musculus

<400> 8

ggccctggaa agctttgaa gag

23

~~11~~ <210> 9

<211> 23

<212> DNA

<213> Homo sapiens

<400> 9

ccccggaaatg gtggcaagta ctg

23

<210> 10

<211> 23

<212> DNA

<213> Homo sapiens

<400> 10

acccacatct gtctgactcc aaa

23

<210> 11

<211> 23

<212> DNA

<213> Homo sapiens

<400> 11

ccagttgggc agtcctcagt gtt

23

<210> 12

<211> 22

<212> DNA

<213> Homo sapiens
<400> 12
ggtcgggtgg gtgggttag gc

22

<210> 13

<211> 17

<212> PRT

<213> Homo sapiens

<400> 13

Cys Ala Ser Leu Ser Arg Phe Val Glu Thr Leu Val Val Ala Asp Asp
1 5 10 15

Lys

<210> 14

<211> 3250

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (121)..(2910)

<400> 14

tgactcaatc ctgcaagcaa gtgtgtgtgt gtcggccatcc cccggccccgt taacttcata 60

gcaaataaca aataccata aagtcccagt cgccgcagcccc ctcccccgcgg gcagcgcact 120

atg ctg ctc ggg tgg gcg tcc ctg ctg ctg tgc gcg ttc cgc ctg ccc 168
Met Leu Leu Gly Trp Ala Ser Leu Leu Leu Cys Ala Phe Arg Leu Pro
1 5 10 15

ctg gcc gcg gtc ggc ccc gcc gcg aca cct gcc cag gat aaa gcc ggg 216
Leu Ala Ala Val Gly Pro Ala Ala Thr Pro Ala Gln Asp Lys Ala Gly
20 25 30

cag cct ccg act gct gca gca gcc cag ccc cgc cgg cgg cag ggg 264
Gln Pro Pro Thr Ala Ala Ala Gln Pro Arg Arg Arg Gln Gly
35 40 45

gag gag gtg cag gag cga gcc gag cct ccc ggc cac ccg cac ccc ctg 312
Glu Glu Val Gln Glu Arg Ala Glu Pro Pro Gly His Pro His Pro Leu
50 55 60

gcg cag cgg cgc agg agc aag ggg ctg gtg cag aac atc gac caa ctc 360

INS
C1

Ala Gln Arg Arg Arg Ser Lys Gly Leu Val Gln Asn Ile Asp Gln Leu
 65 70 75 80

tac tcc ggc ggc ggc aag gtg ggc tac ctc gtc tac gcg ggc ggc cgg 408
 Tyr Ser Gly Gly Lys Val Gly Tyr Leu Val Tyr Ala Gly Gly Arg
 85 90 95

agg ttc ctc ttg gac ctg gag cga gat ggt tcg gtg ggc att gct ggc 456
 Arg Phe Leu Leu Asp Leu Glu Arg Asp Gly Ser Val Gly Ile Ala Gly
 100 105 110

ttc gtg ccc gca gga ggc ggg acg agt gcg ccc tgg cgc cac cgg agc 504
 Phe Val Pro Ala Gly Gly Thr Ser Ala Pro Trp Arg His Arg Ser
 115 120 125

cac tgc ttc tat cgg ggc aca gtg gac gct agt ccc cgc tct ctg gct 552
 His Cys Phe Tyr Arg Gly Thr Val Asp Ala Ser Pro Arg Ser Leu Ala
 130 135 140

gtc ttt gac ctc tgt ggg ggt ctc gac ggc ttc ttc gcg gtc aag cac 600
 Val Phe Asp Leu Cys Gly Leu Asp Gly Phe Phe Ala Val Lys His
 145 150 155 160

gcg cgc tac acc cta aag cca ctg ctg cgc gga ccc tgg gcg gag gaa 648
 Ala Arg Tyr Thr Leu Lys Pro Leu Leu Arg Gly Pro Trp Ala Glu Glu
 165 170 175

gaa aag ggg cgc gtg tac ggg gat ggg tcc gca cgg atc ctg cac gtc 696
 Glu Lys Gly Arg Val Tyr Gly Asp Gly Ser Ala Arg Ile Leu His Val
 180 185 190

tac acc cgc gag ggc ttc agc ttc gag gcc ctg ccg cgc gcc agc 744
 Tyr Thr Arg Glu Gly Phe Ser Phe Glu Ala Leu Pro Pro Arg Ala Ser
 195 200 205

tgc gaa acc ccc gcg tcc aca ccg gag gcc cac gag cat gct ccg gcg 792
 Cys Glu Thr Pro Ala Ser Thr Pro Glu Ala His Glu His Ala Pro Ala
 210 215 220

cac agc aac ccg agc gga cgc gca gca ctg gcc tcg ctc ttg gac 840
 His Ser Asn Pro Ser Gly Arg Ala Ala Leu Ala Ser Gln Leu Leu Asp
 225 230 235 240

cag tcc gct ctc tcg ccc gct ggg ggc tca gga ccg cag acg tgg tgg 888
 Gln Ser Ala Leu Ser Pro Ala Gly Gly Ser Gly Pro Gln Thr Trp Trp
 245 250 255

cgg cgg cgg cgc cgc tcc atc tcc cgg gcc cgc cag gtg gag ctg ctt 936
 Arg Arg Arg Arg Ser Ile Ser Arg Ala Arg Gln Val Glu Leu Leu
 260 265 270

ctg gtg gct gac gcg tcc atg gcg cgg ttg tat ggc cgg ggc ctg cag 984
 Leu Val Ala Asp Ala Ser Met Ala Arg Leu Tyr Gly Arg Gly Leu Gln
 275 280 285

cat tac ctg ctg acc ctg gcc tcc atc gcc aat agg ctg tac agc cat 1032
 His Tyr Leu Leu Thr Leu Ala Ser Ile Ala Asn Arg Leu Tyr Ser His

290 295 300 1080
 gct agc atc gag aac cac atc cgc ctg gcc gtg gtg aag gtg gtg gtg
 Ala Ser Ile Glu Asn His Ile Arg Leu Ala Val Val Lys Val Val Val
 305 310 315 320

 cta gga gac aag gac aag agc ctg gaa gtg agc aag aac gct gcc acc 1128
 Leu Gly Asp Lys Asp Lys Ser Leu Glu Val Ser Lys Asn Ala Ala Thr
 325 330 335

 aca ctc aag aac ttt tgc aag tgg cag cac caa cac aac cag ctg gga 1176
 Thr Leu Lys Asn Phe Cys Lys Trp Gln His Gln His Asn Gln Leu Gly
 340 345 350

 gat gac cat gag gag cac tac gat gca gct atc ctg ttt act cgg gag 1224
 Asp Asp His Glu Glu His Tyr Asp Ala Ala Ile Leu Phe Thr Arg Glu
 355 360 365

 gat tta tgt ggg cat cat tca tgt gac acc ctg gga atg gca gac gtt 1272
 Asp Leu Cys Gly His His Ser Cys Asp Thr Leu Gly Met Ala Asp Val
 370 375 380

 ggg acc ata tgt tct cca gag cgc agc tgt gct gtg att gaa gac gat 1320
 Gly Thr Ile Cys Ser Pro Glu Arg Ser Cys Ala Val Ile Glu Asp Asp
 385 390 395 400

 ggc ctc cac gca gcc ttc act gtg gct cac gaa atc gga cat tta ctt 1368
 Gly Leu His Ala Ala Phe Thr Val Ala His Glu Ile Gly His Leu Leu
 405 410 415

 ggc ctc tcc cat gac gat tcc aaa ttc tgt gaa gag acc ttt ggt tcc 1416
 Gly Leu Ser His Asp Asp Ser Lys Phe Cys Glu Glu Thr Phe Gly Ser
 420 425 430

 aca gaa gat aag cgc tta atg tct tcc atc ctt acc agc att gat gca 1464
 Thr Glu Asp Lys Arg Leu Met Ser Ser Ile Leu Thr Ser Ile Asp Ala
 435 440 445

 tct aag ccc tgg tcc aaa tgc act tca gcc acc atc aca gaa ttc ctg 1512
 Ser Lys Pro Trp Ser Lys Cys Thr Ser Ala Thr Ile Thr Glu Phe Leu
 450 455 460

 gat gat ggc cat ggt aac tgt ttg ctg gac cta cca cga aag cag atc 1560
 Asp Asp Gly His Gly Asn Cys Leu Leu Asp Leu Pro Arg Lys Gln Ile
 465 470 475 480

 ctg ggc ccc gaa gaa ctc cca gga cag acc tac gat gcc acc cag cag 1608
 Leu Gly Pro Glu Glu Leu Pro Gly Gln Thr Tyr Asp Ala Thr Gln Gln
 485 490 495

 tgc aac ctg aca ttc ggg cct gag tac tcc gtg tgt ccc ggc atg gat 1656
 Cys Asn Leu Thr Phe Gly Pro Glu Tyr Ser Val Cys Pro Gly Met Asp
 500 505 510

 gtc tgt gct cgc ctg tgg tgt gct gtg gta cgc cag ggc cag atg gtc 1704
 Val Cys Ala Arg Leu Trp Cys Ala Val Val Arg Gln Gly Gln Met Val
 515 520 525

NS
C

tgc acc aag aag ctg cct gcg gtg gaa ggg acg cct tgt gga aag 1752
 Cys Leu Thr Lys Lys Leu Pro Ala Val Glu Gly Thr Pro Cys Gly Lys
 530 535 540

ggg aga atc tgc ctg cag ggc aaa tgt gtg gac aaa acc aag aaa aaa 1800
 Gly Arg Ile Cys Leu Gln Gly Lys Cys Val Asp Lys Thr Lys Lys Lys
 545 550 555 560

tat tat tca acg tca agc cat ggc aac tgg gga tct tgg gga tcc tgg 1848
 Tyr Tyr Ser Thr Ser Ser His Gly Asn Trp Gly Ser Trp Gly Ser Trp
 565 570 575

ggc cag tgt tcc cgc tca tgt gga gga gta cag ttt gcc tat cgt 1896
 Gly Gln Cys Ser Arg Ser Cys Gly Gly Val Gln Phe Ala Tyr Arg
 580 585 590

I NS C
 cac tgt aat aac cct gct ccc aga aac aac gga cgc tac tgc aca ggg 1944
 His Cys Asn Asn Pro Ala Pro Arg Asn Gly Arg Tyr Cys Thr Gly
 595 600 605

aag agg gcc atc tac cgc tcc tgc agt ctc atg ccc tgc cca ccc aat 1992
 Lys Arg Ala Ile Tyr Arg Ser Cys Ser Leu Met Pro Cys Pro Pro Asn
 610 615 620

ggt aaa tca ttt cgt cat gaa cag tgt gag gcc aaa aat ggc tat cag 2040
 Gly Lys Ser Phe Arg His Glu Gln Cys Glu Ala Lys Asn Gly Tyr Gln
 625 630 635 640

tct gat gca aaa gga gtc aaa act ttt tgc gaa tgg gtt ccc aaa tat 2088
 Ser Asp Ala Lys Gly Val Lys Thr Phe Val Glu Trp Val Pro Lys Tyr
 645 650 655

gca ggt gtc ctg cca gcg gat gtg tgc aag ctg acc tgc aga gcc aag 2136
 Ala Gly Val Leu Pro Ala Asp Val Cys Lys Leu Thr Cys Arg Ala Lys
 660 665 670

ggc act ggc tac tat gtg gta ttt tct cca aag gtg acc gat ggc act 2184
 Gly Thr Gly Tyr Val Val Phe Ser Pro Lys Val Thr Asp Gly Thr
 675 680 685

gaa tgt agg ccg tac agt aat tcc gtc tgc gtc cgg ggg aag tgt gtg 2232
 Glu Cys Arg Pro Tyr Ser Asn Ser Val Cys Val Arg Gly Lys Cys Val
 690 695 700

aga act ggc tgt gac ggc atc att ggc tca aag ctg cag tat gac aag 2280
 Arg Thr Gly Cys Asp Gly Ile Ile Gly Ser Lys Leu Gln Tyr Asp Lys
 705 710 715 720

tgc gga gta tgt gga gga gac aac tcc agc tgt aca aag att gtt gga 2328
 Cys Gly Val Cys Gly Gly Asp Asn Ser Ser Cys Thr Lys Ile Val Gly
 725 730 735

acc ttt aat aag aaa agt aag ggt tac act gac gtg gtg agg att cct 2376
 Thr Phe Asn Lys Lys Ser Lys Gly Tyr Thr Asp Val Val Arg Ile Pro
 740 745 750

1NS
1CD

gaa ggg gca acc cac ata aaa gtt cga cag ttc aaa gcc aaa gac cag Glu Gly Ala Thr His Ile Lys Val Arg Gln Phe Lys Ala Lys Asp Gln 755 760 765	2424
act aga ttc act gcc tat tta gcc ctg aaa aag aaa aac ggt gag tac Thr Arg Phe Thr Ala Tyr Leu Ala Leu Lys Lys Asn Gly Glu Tyr 770 775 780	2472
ctt atc aat gga aag tac atg atc tcc act tca gag act atc att gac Leu Ile Asn Gly Lys Tyr Met Ile Ser Thr Ser Glu Thr Ile Ile Asp 785 790 795 800	2520
atc aat gga aca gtc atg aac tat agc ggt tgg agc cac agg gat gac Ile Asn Gly Thr Val Met Asn Tyr Ser Gly Trp Ser His Arg Asp Asp 805 810 815	2568
ttc ctg cat ggc atg ggc tac tct gcc acg aag gaa att cta ata gtg Phe Leu His Gly Met Gly Tyr Ser Ala Thr Lys Glu Ile Leu Ile Val 820 825 830	2616
cag att ctt gca aca gac ccc act aaa cca tta gat gtc cgt tat agc Gln Ile Leu Ala Thr Asp Pro Thr Lys Pro Leu Asp Val Arg Tyr Ser 835 840 845	2664
ttt ttt gtt ccc aag aag tcc act cca aaa gta aac tct gtc act agt Phe Phe Val Pro Lys Lys Ser Thr Pro Lys Val Asn Ser Val Thr Ser 850 855 860	2712
cat ggc agc aat aaa gtg gga tca cac act tcg cag ccg cag tgg gtc His Gly Ser Asn Lys Val Gly Ser His Thr Ser Gln Pro Gln Trp Val 865 870 875 880	2760
acg ggc cca tgg ctc gcc tgc tct agg acc tgt gac aca ggt tgg cac Thr Gly Pro Trp Leu Ala Cys Ser Arg Thr Cys Asp Thr Gly Trp His 885 890 895	2808
acc aga acg gtg cag tgc cag gat gga aac cgg aag tta gca aaa gga Thr Arg Thr Val Gln Cys Gln Asp Gly Asn Arg Lys Leu Ala Lys Gly 900 905 910	2856
tgt cct ctc tcc caa agg cct tct gcg ttt aag caa tgc ttg ttg aag Cys Pro Leu Ser Gln Arg Pro Ser Ala Phe Lys Gln Cys Leu Leu Lys 915 920 925	2904
aaa tgt tagcctgtgg ttatgatctt atgcacaaag ataactggag gattcagcac Lys Cys 930	2960
cgtatgcagtc gtggtaaca ggaggctac ctaacgcaca gaaagtcatg cttcagtgac	3020
attgtcaaca ggagtccaat tatgggcaga atctgcttc tgtgaccaaa agaggatgtg	3080
cactgctca cgtgacagtg gtgaccttc aatatagaaa aacttggag ttattgaaca	3140
tccccctggaa ttacaagaaa cactgatgaa tgtaaatca gggacattt gaagatggca	3200
gaactgtctc ccccttgtca cctacacctg aatagaatgt cttaatgg	3250

<210> 15

<211> 930

<212> PRT

<213> Homo sapiens

<400> 15

Met Leu Leu Gly Trp Ala Ser Leu Leu Leu Cys Ala Phe Arg Leu Pro
1 5 10 15

Leu Ala Ala Val Gly Pro Ala Ala Thr Pro Ala Gln Asp Lys Ala Gly
20 25 30

Gln Pro Pro Thr Ala Ala Ala Ala Gln Pro Arg Arg Arg Gln Gly
35 40 45

Glu Glu Val Gln Glu Arg Ala Glu Pro Pro Gly His Pro His Pro Leu
50 55 60

Ala Gln Arg Arg Arg Ser Lys Gly Leu Val Gln Asn Ile Asp Gln Leu
65 70 75 80

Tyr Ser Gly Gly Lys Val Gly Tyr Leu Val Tyr Ala Gly Gly Arg
85 90 95

Arg Phe Leu Leu Asp Leu Glu Arg Asp Gly Ser Val Gly Ile Ala Gly
100 105 110

Phe Val Pro Ala Gly Gly Thr Ser Ala Pro Trp Arg His Arg Ser
115 120 125

His Cys Phe Tyr Arg Gly Thr Val Asp Ala Ser Pro Arg Ser Leu Ala
130 135 140

Val Phe Asp Leu Cys Gly Gly Leu Asp Gly Phe Phe Ala Val Lys His
145 150 155 160

Ala Arg Tyr Thr Leu Lys Pro Leu Leu Arg Gly Pro Trp Ala Glu Glu
165 170 175

Glu Lys Gly Arg Val Tyr Gly Asp Gly Ser Ala Arg Ile Leu His Val
180 185 190

Tyr Thr Arg Glu Gly Phe Ser Phe Glu Ala Leu Pro Pro Arg Ala Ser
195 200 205

Cys Glu Thr Pro Ala Ser Thr Pro Glu Ala His Glu His Ala Pro Ala
210 215 220

His Ser Asn Pro Ser Gly Arg Ala Ala Leu Ala Ser Gln Leu Leu Asp
225 230 235 240

Gln Ser Ala Leu Ser Pro Ala Gly Gly Ser Gly Pro Gln Thr Trp Trp

245 250 255

Arg Arg Arg Arg Arg Ser Ile Ser Arg Ala Arg Gln Val Glu Leu Leu
260 265 270

Leu Val Ala Asp Ala Ser Met Ala Arg Leu Tyr Gly Arg Gly Leu Gln
275 280 285

His Tyr Leu Leu Thr Leu Ala Ser Ile Ala Asn Arg Leu Tyr Ser His
290 295 300

Ala Ser Ile Glu Asn His Ile Arg Leu Ala Val Val Lys Val Val Val
305 310 315 320

Leu Gly Asp Lys Asp Lys Ser Leu Glu Val Ser Lys Asn Ala Ala Thr
325 330 335

Thr Leu Lys Asn Phe Cys Lys Trp Gln His Gln His Asn Gln Leu Gly
340 345 350

Asp Asp His Glu Glu His Tyr Asp Ala Ala Ile Leu Phe Thr Arg Glu
355 360 365

Asp Leu Cys Gly His His Ser Cys Asp Thr Leu Gly Met Ala Asp Val
370 375 380

Gly Thr Ile Cys Ser Pro Glu Arg Ser Cys Ala Val Ile Glu Asp Asp
385 390 395 400

Gly Leu His Ala Ala Phe Thr Val Ala His Glu Ile Gly His Leu Leu
405 410 415

Gly Leu Ser His Asp Asp Ser Lys Phe Cys Glu Glu Thr Phe Gly Ser
420 425 430

Thr Glu Asp Lys Arg Leu Met Ser Ser Ile Leu Thr Ser Ile Asp Ala
435 440 445

Ser Lys Pro Trp Ser Lys Cys Thr Ser Ala Thr Ile Thr Glu Phe Leu
450 455 460

Asp Asp Gly His Gly Asn Cys Leu Leu Asp Leu Pro Arg Lys Gln Ile
465 470 475 480

Leu Gly Pro Glu Glu Leu Pro Gly Gln Thr Tyr Asp Ala Thr Gln Gln
485 490 495

Cys Asn Leu Thr Phe Gly Pro Glu Tyr Ser Val Cys Pro Gly Met Asp
500 505 510

Val Cys Ala Arg Leu Trp Cys Ala Val Val Arg Gln Gly Gln Met Val
515 520 525

Cys Leu Thr Lys Lys Leu Pro Ala Val Glu Gly Thr Pro Cys Gly Lys
530 535 540

Gly Arg Ile Cys Leu Gln Gly Lys Cys Val Asp Lys Thr Lys Lys

850 855 860

His Gly Ser Asn Lys Val Gly Ser His Thr Ser Gln Pro Gln Trp Val
865 870 875 880

Thr Gly Pro Trp Leu Ala Cys Ser Arg Thr Cys Asp Thr Gly Trp His
885 890 895

Thr Arg Thr Val Gln Cys Gln Asp Gly Asn Arg Lys Leu Ala Lys Gly
900 905 910

Cys Pro Leu Ser Gln Arg Pro Ser Ala Phe Lys Gln Cys Leu Leu Lys
915 920 925

Lys Cys
930

<210> 16

<211> 42

<212> PRT

<213> Homo sapiens

<400> 16

Ser Ile Ser Arg Ala Arg Gln Val Glu Leu Leu Leu Val Ala Asp Ala
1 5 10 15

Ser Met Ala Arg Met Tyr Gly Arg Gly Leu Gln His Tyr Leu Leu Thr
20 25 30

Leu Ala Ser Ile Ala Asn Lys Leu Tyr Phe
35 40

<210> 17

<211> 23

<212> DNA

<213> Mus musculus

<400> 17
cggccacgac cctcaagaac ttt 23

<210> 18

<211> 25

<212> DNA

<213> Mus musculus

<400> 18
gcatggaggc catcatcttc aatca 25

INS

<210> 19
<211> 22
<212> DNA
<213> Homo sapiens
<400> 19
gggaggattt atgtgggcat ca
<210> 20
<211> 23
<212> DNA
<213> Homo sapiens
<400> 20
gtgcatttgg accagggctt aga
<210> 21
<211> 13
<212> PRT
<213> artificial
<220>
<223> Synthesized peptide.
<220>
<221> MOD_RES
<222> (12)...(12)
<223> Acp
<400> 21

Ser Ile Ser Arg Ala Arg Gln Val Glu Leu Leu Xaa Cys
1 5 10

22

23